PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
Jeffrey D. Hsi
EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

	Date of mailing *(day/month/year)* 29 AUG 2008
Applicant's or agent's file reference 66643WO (51035)	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US 07/23984	International filing date *(day/month/year)* 15 November 2007 (15.11.2007)
Applicant HAAS, JOHN I.	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 740 1435

   For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   ☐ *the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.*

   ☐ *no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.*

4. **Reminders**

   Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

   In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

   See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/220 (January 2004) *(See notes on accompanying sheet)*

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 66643WO (51035)	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US 07/23984	*International filing date (day/month/year)* 15 November 2007 (15.11.2007)	*(Earliest) Priority Date (day/month/year)* 15 November 2006 (15.11.2006)
Applicant HAAS, JOHN I.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 1X sheets.

☐ *It is also accompanied by a copy of each prior art document cited in this report.*

1. ***Basis of the report***

   a. With regard to the **language**, the international search was carried out on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

   b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** *authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a))*.

   c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ ***Certain claims were found unsearchable*** *(see Box No. II)*.

3. ☐ **Unity of invention is lacking** (see Box No. III).

4. With regard to the **title**,

   ☒ the text is approved as submitted by the applicant.

   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

   ☒ the text is approved as submitted by the applicant.

   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. *With regard to the* **drawings**,

   a. the figure of the **drawings** to be published with the abstract is Figure No. 1

   ☒ as suggested by the applicant.

   ☐ as selected by this Authority, because the applicant failed to suggest a figure.

   ☐ *as selected by this Authority, because this figure better characterizes the invention.*

   b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 07/23984

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 25-27 and 50-61
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-24, 28-49 and 62-64, drawn to a method comprising contacting the pathogen with an effective amount of a composition comprising a hop derivative (claims 1-24) and a composition for treating or preventing a honey bee pathogen infection and/or hive infestation, the composition comprising an effective amount of a hop derivative in a suitable form for delivery to a bee or hive (claims 28-49 and 62-64).

- Please see extra sheet for continuation -

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-24, 28-49 and 62-64

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 07/23984

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A01K 51/00 (2008.04)
USPC - 449/2
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC : 449/2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC : 449/2, 449/1, 449/3: keyword search, as below

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Google Scholar, USPTO West (databases: PGPB,USPT,USOC,EPAB,JPAB) - Search Terms: honey, bee, infection, infestation, treatment, acid, alpha, beta, hops, humulone, lupulone, galleria, wax moth, moth, lepidoptera, paenibacillus, melissococcus, fungal, parasite, pathogen, ascosphaera, foulbrood, chalkbrood

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6,096,350 A (KEMP et al.) 1 August 2000 (01.08.2000) abstract; col 1, ln 45-46; col 9, ln 55-56; col 1, ln 24-44	1-24, 28-49, 62-64
Y	US 2005/0220914 A1 (PROBASCO et al.) 6 October 2005 (06.10.2005) abstract; para [0014]; [0009]; [0010]; [0007]; [0018]; [0020]; [0015]; [0011]; [0018]	1-18, 22-24, 28-49 and 62-64
Y	US 2005/0049230 A1 (HENRICH et al.) 3 March 2005 (03.03.2005) para [0065]; [0154]	19-21
Y	US 2006/0013870 A1 (KUHRTS) 19 January 2006 (19.01.2006) abstract; para [0059]	6, 7, 8, 13 and 14
Y	US 2006/0009122 A1 (SWANSON) 12 January 2006 (12.01.2006) abstract; para [0045]	45-49

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 August 2008 (20.08.2008)	29 AUG 2008
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)

Continuation of Box III:

Group II, claims 65-81, drawn to a method of identifying a hop derivative that inhibits a bacterial or fungal pathogen, the method comprising
(a) contacting a bacterial or fungal culture with a test composition comprising a hop derivative; and
(b) assaying bacterial or fungal growth.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The screening method for identifying a hop derivative that inhibits a bacterial or fungal pathogen is not a method of using a composition comprising a hop derivative. In the absence of any teaching as to the structure required for a compound to act as a biocide, there is no single general concept that links the screening method to the claimed hop derivatives and methods of their use. Thus, unity of invention is lacking.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
Jeffrey D. Hsi
EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	29 AUG 2008
Applicant's or agent's file reference 66643WO (51035)	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 07/23984	15 November 2007 (15.11.2007)	15 November 2006 (15.11.2006)

International Patent Classification (IPC) or both national classification and IPC
IPC(8) - A01K 51/00 (2008.04)
USPC - 449/2

Applicant HAAS, JOHN I.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/US	Date of completion of this opinion	Authorized officer:
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	20 August 2008 (20.08.2008)	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/237 (cover sheet) (April 2007)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 07/23984

Box No. I **Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. *format of material*

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing

      ☐ *contained in the international application as filed*

      ☐ filed together with the international application in electronic form

      ☐ furnished subsequently to this Authority for the purposes of search

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. *Additional comments:*

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 07/23984

Box No. III ***Non-establishment of opinion with regard to novelty, inventive step and industrial applicability***

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 25-27 and 50-61

because: improper multiple dependent claims

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international search *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 25-27 and 50-61 are so unclear that no meaningful opinion could be formed *(specify)*:
claims are not drafted in accordance with the second and third sentences of Rule 6.4 (a) regarding multiply dependent claims.

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for said claims Nos. 25-27 and 50-61

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, *if in electronic form only*, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 07/23984

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the appicable time limit:

   ☐ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☒ not paid additional fees

2. ☐ *This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.*

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ *complied with*

   ☒ not complied with for the following reasons:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-24, 28-49 and 62-64, drawn to a method comprising contacting the pathogen with an effective amount of a composition comprising a hop derivative (claims 1-24) and a composition for treating or preventing a honey bee pathogen infection and/or hive infestation, the composition comprising an effective amount of a hop derivative in a suitable form for delivery to a bee or hive (claims 28-49 and 62-64).

Group II, claims 65-81, drawn to a method of identifying a hop derivative that inhibits a bacterial or fungal pathogen, the method comprising
(a) contacting a bacterial or fungal culture with a test composition comprising a hop derivative; and
(b) assaying bacterial or fungal growth.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The screening method for identifying a hop derivative that inhibits a bacterial or fungal pathogen is not a method of using a composition comprising a hop derivative. In the absence of any teaching as to the structure required for a compound to act as a biocide, there is no single general concept that links the screening method to the claimed hop derivatives and methods of their use. Thus, unity of invention is lacking.

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☐ all parts

   ☒ the parts relating to claims Nos. 1-24, 28-49 and 62-64

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 07/23984

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-24, 28-49 and 62-64	YES
	Claims	None	NO
Inventive step (IS)	Claims	None	YES
	Claims	1-24, 28-49 and 62-64	NO
Industrial applicability (IA)	Claims	1-24, 28-49 and 62-64	YES
	Claims	None	NO

2. Citations and explanations:

Claims 1, 2-4, 5, 9-12, 15-18, 22-24, 28-44 and 62-64 lack an inventive step under PCT Article 33(3) as being obvious over US 6,096,350 A to Kemp et al. (hereinafter "Kemp") in view of US 2005/0220914 A1 to Probasco et al. (hereinafter "Probasco").

As to Claim 1, Kemp discloses a method of inhibiting a honey bee pathogen, the method comprising contacting the pathogen with an effective amount of a composition controlling a honey bee pathogen (abstract). Although Kemp does not explicitly teach wherein the agent comprises a hop derivative, Probasco teaches a composition comprising a hop derivative (abstract) useful for treating mildews (para [0014]) and fungal infestations (para [0009]), which Kemp teaches were known to be bee pathogens (abstract). It would have been obvious to a person skilled in the art to apply a known pathogen inhibitor or pathogenicidal preparation, as taught by Probasco, to a bee pathogen, as taught by Kemp, in order to reduce the toxicity of the treatment regimen (Probasco teaches wherein the hop derivatives are generally recognized as safe; para [0010]).

As to Claim 5, Kemp discloses a method of treating or preventing a pathogen infection in a honey bee hive, the method comprising contacting the hive with an effective amount of a composition comprising a treating agent, thereby treating or preventing a pathogen infection in a honey bee hive (abstract). Although Kemp does not explicitly teach wherein the agent comprises a hop derivative, Probasco teaches a composition comprising a hop derivative (abstract) useful for treating mildews (para [0014]) and fungal infestations (para [0009]), which Kemp teaches were known to be bee pathogens (abstract). It would have been obvious to a person skilled in the art to apply a known pathogen inhibitor or pathogenicidal preparation, as taught by Probasco, to a bee pathogen, as taught by Kemp, in order to reduce the toxicity of the treatment regimen (Probasco teaches wherein the hop derivatives are generally recognized as safe; para [0010]).

As to Claims 2 and 9, Probasco teaches wherein the pathogen is a bacterial or fungal pathogen (fungal; para [0009]).

As to Claim 3, Kemp teaches wherein the bacterial pathogen is Melissococcus pluton or Paenibacillus larvae (col 1, ln 24-44).

As to Claims 4 and 10, Kemp teaches wherein the fungal pathogen is Ascosphaera apis (col 1, ln 45-46).

As to Claim 11, Probasco discloses wherein the hop derivative is an alpha acid (para [0007])

As to Claim 12, Probasco discloses wherein the composition comprises at least 1,000 ppm alpha or beta acids (para [0018]).

As to Claim 15, Probasco discloses wherein the composition comprises a combination of alpha and beta acids (para [0007]).

As to Claim 16, although Probasco does not explicitly teach wherein the composition comprises at least 1000 ppm beta acid and 1000 *ppm alpha acids, Probasco teaches the use of up to 10% of alpha or beta acids (para [0018]). It would have been obvious to a person* skilled in the art to use at least 1000 ppm of both acids in a mixture thereof, as taught by Probasco, in order to test a reasonable range of concentrations or ratios of the acids in order to produce a desired ameliorative effect.

As to Claims 17 and 18, Probasco discloses wherein the contacting inhibits the growth or proliferation of a bacteria or fungus, or kills the bacteria or fungus (para [0009], pesticide; para [0020]).

As to Claim 22, Kemp teaches a method for maintaining the health of a honey bee hive, the method comprising: contacting the hive with an effective amount of a composition comprising a treatment agent, thereby maintaining the health of the honey bee hive (abstract). Although Kemp does not explicitly teach wherein the agent comprises a hop derivative, Probasco teaches a composition comprising a hop derivative (abstract) useful for treating mildews (para [0014]) and fungal infestations (para [0009]), which Kemp teaches were known to be bee pathogens (abstract). It would have been obvious to a person skilled in the art to apply a known pathogen inhibitor or pathogenicidal preparation, as taught by Probasco, to a bee hive, as taught by Kemp, in order to prevent infection or infestation of the hive, as taught by Kemp (abstract) using the hop derivative to reduce the toxicity of the treatment regimen (Probasco teaches wherein the hop derivatives *are generally recognized as safe; para [0010]).*

As to Claims 23, and 24, Kemp teaches wherein the hive is maintained in an essentially pathogen-free state or infestation-free state (complete freedom from infection; col 9, ln 55-56).

- Please see first continuation sheet -

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:
Box V.2: Citations and Explanations -

As to Claim 28, Kemp discloses a composition for treating or preventing a honey bee pathogen infection and/or hive infestation, the composition comprising an effective amount of an active agent in a suitable form for delivery to a bee or hive (abstract). Although Kemp does not explicitly teach wherein the agent comprises a hop derivative, Probasco teaches a composition comprising a hop derivative (abstract) useful for treating mildews (para [0014]) and fungal infestations (para [0009]), which Kemp teaches were known to be bee pathogens (abstract). It would have been obvious to a person skilled in the art to apply a known pathogen inhibitor or pathogenicidal preparation, as taught by Probasco, to a bee hive, as taught by Kemp, in order to prevent infection or infestation of the hive, as taught by Kemp (abstract) using the hop derivative to reduce the toxicity of the treatment regimen (Probasco teaches wherein the hop derivatives are generally recognized as safe; para [0010]).

As to Claim 29, Probasco discloses wherein the effective amount inhibits the growth, proliferation, or survival of a bacterial or fungal pathogen (para [0009])

As to Claim 30, Probasco discloses wherein the effective amount controls an acarid or destructive insect (para [0008]).

As to Claims 31 and 38, Probasco discloses wherein the hop derivative is an alpha acid, beta acid, or combination of an alpha and a beta acid (para [0007]).

As to Claims 32-37, 39, 43 and 44, Probasco teaches wherein initial tests were performed using 10% of either alpha or beta acids (para [0018]). It would have been obvious to a person skilled in the art to increase or decrease the amounts of either or both acids in order to achieve a desired preventative effect or treatment based on routine experimentation and the teaching of Probasco.

As to Claim 40, Probasco discloses wherein the form is selected from the group consisting of a liquid, a powder, an oil, an emulsion, a capsule, and a vapor (para [0015]).

As to Claim 41, Probasco discloses wherein the composition further comprises a carrier medium (para [0011])

As to Claim 42, although neither Probasco nor Kemp explicitly teaches wherein the composition comprises a sodium or magnesium salt of beta acids, Probasco teaches wherein "stable aqueous solutions of certain hop acids can be prepared by the selection of appropriate concentration and pH" (para [0016]). It would have been obvious to a person skilled in the art that adjustment of pH with an acid would have been performed via titration, producing a salt. It further would have been obvious to use a common counter-ion, such as sodium for said salt.

As to Claim 62, although neither Kemp nor Probasco explicitly teaches a kit for the treatment or prevention of a pathogen infection or hive infestation, the kit comprising an effective amount of a hop derivative in a form suitable for delivery to a site of infection or infestation, Kemp teaches a method of inhibiting a honey bee pathogen, the method comprising contacting the pathogen with an effective amount of a composition controlling a honey bee pathogen (abstract). Although Kemp does not explicitly teach wherein the agent comprises a hop derivative, Probasco teaches a composition comprising a hop derivative (abstract) useful for treating mildews (para [0014]) and fungal infestations (para [0009]), which Kemp teaches were known to be bee pathogens (abstract). It would have been obvious to a person skilled in the art to apply a known pathogen inhibitor or pathogenicidal preparation, as taught by Probasco, to a bee pathogen, as taught by Kemp, in order to reduce the toxicity of the treatment regimen (Probasco teaches wherein the hop derivatives are generally recognized as safe; para [0010]), and to supply said reagents in a kit in order to assure proper utilization.

As to Claims 63 and 64, Kemp teaches wherein the site of infection or infestation is a bee hive or bee (abstract).

Claims 19-21, lack an inventive step under PCT Article 33(3) as being obvious over US 2005/0049230 A1 to Henrich et al. (hereinafter "Henrich") in view of Kemp.

As to Claim 19, Henrich discloses a method of treating or preventing a Lepidoptera infestation (para [0065]), the method comprising contacting the source with an effective amount of a composition comprising a hop derivative, thereby treating or preventing a Lepidoptera infestation (insecticides based upon their ability to activate EcR and/or FXR mediated transcription; abstract - polyketides that increase FXR-dependent transcription, and/or increase or potentiate EcR-mediated transcription, comprise humulone; para [0154] – wherein humulone was known to those skilled in the art to be the chemical name for alpha acids derived from hops). Although Henrich does not explicitly teach wherein the treatment may be applied to a honey bee hive, in a similar invention, Kemp teaches treatment of a honey bee hive with an agent effective to treat parasites (abstract). It would have been obvious to a person skilled in the art to apply an agent capable of preventing a lepidoptera infestation, as taught by Henrich, to a bee hive, as taught by Kemp, in order to control the common infestation of bee hives by lepidoptera.

As to Claims 20 and 21, although neither Henrich nor Kemp explicitly teaches wherein the Lepidoptera is the wax moth, Galleria mellonella,and, therefore, wherein the method treats galleriasis, since Henrich teaches the application of the hop derivative to different species of Lepidoptera (para [0065]). It would have been obvious to a person skilled in the art to apply it to Galleria with a reasonable expectation of success.

- Please see second continuation sheet -

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:
Box V.2: Citations and Explanations (second continuation sheet)

Claims 6, 7, 8, 13 and 14 lack an inventive step under PCT Article 33(3) as being obvious over Kemp in view of Probasco, and further in view of US 2006/0013870 A1 (Kuhrts)

As to Claim 6, Kemp teaches wherein the pathogen infection is a bacterial infection (col 1, ln 24-44). Although Probasco does not explicitly teach wherein a hop derivative may be useful in treating a bacterial infection, Kuhrts teaches a pharmaceutical preparation comprising hop derivatives (abstract) useful as an antibiotic (para [0059]). It would have been obvious to a person skilled in the art to use a hop derivative, as taught by Probasco and Kuhrts, to treat a bacterial infection of bees in a hive, as taught by Kemp, in view of the teaching Kuhrts, in order to utilize an active agent which is safe for the bees, but effective against the infection.

As to Claim 7, Kemp teaches wherein the bacterial pathogen is Melissococcus pluton or Paenibacillus larvae (col 1, ln 24-44).

As to Claim 8, Kemp teaches wherein the infection is American or European foulbrood (col 1, ln 24).

As to Claims 13-14, Probasco discloses wherein the composition comprises at least 1% or 5% alpha or beta acids (para [0018]).

Claims 45-49 lack an inventive step under PCT Article 33(3) as being obvious over Kemp in view of Probasco and further in view of US 2006/0009122 A1 (Swanson)

As to Claim 45, Kemp discloses a composition for treating or preventing a honey bee pathogen infection and/or hive infestation, the composition comprising an effective amount of an active agent in a suitable form for delivery to a honey bee or honey bee hive (abstract). Although Kemp does not explicitly teach wherein the agent comprises a hop derivative, Probasco teaches a composition comprising a hop derivative (abstract) useful for treating mildews (para [0014]) and fungal infestations (para [0009]), which Kemp teaches were known to be bee pathogens (abstract).
Further, although niether Kemp nor Probasco explicitly teaches wherein the formulation comprises an extended release formulation, Kemp teaches wherein the formulation may comprise a gelling agent (abstract). Additionally, Swanson discloses a formulation for extended release treatment of a honey bee hive comprising a cross-linked gelling agent (abstract). It would have been obvious to a person skilled in the art to use a cross-linked gelling formula, as taught by Swanson, with a gelling agent for treatment of a bee hive, as taught by Kemp, using a hop derivative, as taught by Probasco, in order to prevent infection or infestation of the hive, as taught by Kemp (abstract) using the hop deriviative to reduce the toxicity of the treatment regimen (Probasco teaches wherein the hop derivatives are generally recognized as safe; para [0010]).

As to Claim 46, Probasco discloses wherein the effective amount inhibits the growth, proliferation, or survival of a bacterial or fungal pathogen (para [0009]).

As to Claim 47, Probasco teaches wherein the effective amount controls an acarid or destructive insect (para [0008]).

As to Claims 48 and 49, wherein the hop derivative is released over the course of at least 14 days, or 41 days, Swanson teaches wherein "in preferred embodiments, the compositions are stable for a period of several months, or six months or more, or a year or more" (para [0045]).

Claims 1-24, 28-49 and 62-64 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article," "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Volume I/A, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the international application may be amended ?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Preliminary Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where *not to file* the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.